

REMARKS

Reconsideration and withdrawal of the rejections of the Office Action are respectfully requested in view of the remarks and amendments herein. The Examiner is thanked for withdrawing the election of species requirement.

I. STATUS OF THE CLAIMS AND FORMAL MATTERS

Claims 3, 6-7, 11-15, 20-31, 33-34, 37-39, 41 and 42 are now pending. Claims 3, 25, 26, 33 and 37 have been amended, and claims 1, 2, 4, 5, 35 and 36 have been cancelled, without prejudice, without admission, without surrender of subject matter, and without any intention of creating any estoppel as to equivalents.

No new matter is added.

It is submitted that these claims are and were in full compliance with the requirements of 35 U.S.C. §112. In addition, the amendment and remarks herein are not made for the purpose of patentability within the meaning of 35 U.S.C. §§101, 102, 103 or 112; but rather the amendments and remarks herein are made simply for clarification and to round out the scope of protection to which Applicants are entitled.

II. THE REJECTIONS UNDER 35 U.S.C. 112 ARE OVERCOME

Claims 1-7, 11-15, 20-31, 33-39, 41 and 42 were rejected under 35 U.S.C. §112, first paragraph, as allegedly lacking enablement. The rejection is respectfully traversed.

The enablement rejection was based on the allegation that "it is not apparent if the biological material is available to the public". Office Action at 3. The Examiner's attention is respectfully directed to page 5 of the present specification, lines 30-34, which states "Salivaricin B BLIS-producing strains with activity against anaerobic bacteria include K12, and K30 both deposited with Deutsche Sammlung von Mikroorganismen Und Zellkulturen GmbH, Mascheroder Weg 1 b, D-38124, Braunschweig, Germany on 8 October 1999, and 8 October 1999, and assigned Accession Nos. DSM 13084 and 13085 respectively."

Thus, the deposit information for BLIS-producing strains K12, K30, and Sal 20P3 is present in the Office Action. Further, the strains have been made available to the public under the Budapest Treaty following the grant of US Patent No. 6,773,912, the first patent in which these

strains were provided. The specification has been amended herein to indicate that the deposits were made under the Budapest Treaty.

Accordingly, reconsideration and withdrawal of the rejections under 35 U.S.C. §112, first paragraph, is respectfully requested.

Claims 1-7, 11-15, 20-31, 33-39, 41 and 42 were rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter of the invention. The rejection is respectfully traversed.

The indefiniteness rejection was based on the phrases “extract thereof” and “wherein the secondary antibacterial agent(s) are selected from bacteriocin-like inhibitory substance(s)”. Although Applicants believe the phrase “extract thereof” is sufficiently clear, Applicants have removed the phrase from the pending claims. Further, Applicants have amended the claims to specify that the “secondary antibacterial agents” are “additional” to the BLIS-producing *S. salivarius*, or composition comprising said *S. salivarius*, as described in claim 3. Thus, Applicants believe the indefiniteness rejections are moot in view of the amendments herein.

Accordingly, reconsideration and withdrawal of the rejections under 35 U.S.C. §112, second paragraph, are respectfully requested.

III. THE ART REJECTIONS ARE OVERCOME

Claims 1-7, 11-15 and 20-30 were rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Tagg et al. Claims 1-7, 11-15, 20-31, 33-39, 41 and 42 were rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Tagg et al. in view of Huatan et al. and Chikindas et al., and further in view of Kross.

It is respectfully asserted that a two-prong inquiry must be satisfied in order for a Section 102 rejection to stand. First, the prior art reference must contain all of the elements of the claimed invention. See *Lewmar Marine Inc. v. Bariant Inc.*, 3 U.S.P.Q.2d 1766 (Fed. Cir. 1987). Second, the prior art must contain an enabling disclosure. See *Chester v. Miller*, 15 U.S.P.Q.2d 1333, 1336 (Fed. Cir. 1990). A reference contains an enabling disclosure if a person of ordinary skill in the art could have combined the description of the invention in the prior art reference with his own knowledge of the art to have placed himself in possession of the invention. See *In re Donohue*, 226, U.S.P.Q. 619, 621 (Fed. Cir. 1985).

Initially, Applicants respectfully assert that WO 01/27143 fails to teach each and every element of the pending claims.

The Examiner is also respectfully reminded of the case law as to obviousness, namely, that there must be some prior art teaching which would have provided the necessary incentive or motivation for modifying the reference teachings. *In re Laskowski*, 12 U.S.P.Q. 2d 1397, 1399 (Fed. Cir. 1989); *In re Obukowitz*, 27 U.S.P.Q. 2d 1063 (BOPAI 1993). Further still, "obvious to try" is not the standard under 35 U.S.C. §103. *In re Fine*, 5 U.S.P.Q. 2d 1596, 1599 (Fed. Cir. 1988). And, as stated by the Court in *In re Fritch*, 23 U.S.P.Q. 2d 1780, 1783-1784 (Fed. Cir. 1992): "The mere fact that the prior art may be modified in the manner suggested by the Office Action does not make the modification obvious unless the prior art suggests the desirability of the modification."

Also, the Examiner is respectfully reminded that for the Section 103 rejection to be proper, both the suggestion of the claimed invention and the expectation of success must be founded in the prior art, and not Applicants' disclosure. *In re Dow*, 5 U.S.P.Q.2d 1529, 1531 (Fed. Cir. 1988). Furthermore, it has recently been reaffirmed by the Supreme Court in *KSR* that the factors set out in *Graham v. John Deere Co. of Kansas City*, 383 U.S. 1, 17-18: "[T]he scope and content of the prior art are determined; differences between the prior art and the claims at issue are...ascertained; and the level of ordinary skill in the pertinent art resolved. Against this background the obviousness or nonobviousness of the subject matter is determined. Such secondary considerations as commercial success, long felt but unsolved needs, failure of others, etc., might be utilized to give light to the circumstances surrounding the origin of the subject matter sought to be patented." *KSR International Co. v. Teleflex Inc.*, 550 U.S. ____ (2007).

Applicants also respectfully assert that none of the cited reference teach or suggest the claimed invention, and that none of the references remedy the deficiencies of WO 01/27143.

The Office Action states that the pending claims are anticipated by WO 01/27143, Applicants' earlier lantibiotic application. The Office Action alleges that K12 and/or K30, when used in the upper respiratory tract, would inherently contact anaerobic bacteria and prophylactically treat halitosis.

Applicants respectfully submit that the pending claims have been amended herein, such that the claims relate to the therapeutic treatment of halitosis, not prophylactics. Thus, claim 3 now requires "a method of treating halitosis in an individual in need thereof, the method

comprising administering to said individual a BLIS-producing *S. salivarius*, or composition comprising said *S. salivarius*, effective to at least inhibit growth of anaerobic bacteria in the oral cavity of the individual."

Applicants respectfully submit that support for the amended recitation is found in claims 1-4 as originally presented. Further, Applicants respectfully submit that nothing in WO 01/27143 teaches the use of BLIS-producing *S. salivarius* to treat halitosis in a subject in need thereof, such that the pending claims are allowable over WO 01/27143. Indeed, the Office Action recognized this deficiency of WO 01/27143, stating at page 9 that "Tagg et al. do not expressly teach treating halitosis with such BLIS-producing *S. salivarius* strains, extracts, or compositions thereof." As such treatment of halitosis is required by the pending claims, Applicants submit that the Section 102 rejections are now moot.

Accordingly, reconsideration and withdrawal of the Section 102 rejection over WO 01/27143 is respectfully requested.

Turning now to the Section 103 rejections, it is again noted that the pending claims have been amended such that the claims require "a method of treating halitosis in an individual in need thereof, the method comprising administering to said individual a BLIS-producing *S. salivarius*, or composition comprising said *S. salivarius*, effective to at least inhibit growth of anaerobic bacteria in the oral cavity of the individual."

Applicants note that the Office Action admits that "Tagg et al. do not expressly teach treating halitosis with such BLIS-producing *S. salivarius* strains, extracts, or compositions thereof." Office Action at 9.

WO 01/27143 relates to *S. salivarius* producing Salivaricin B. The reference also relates to the organisms being useful to colonize the mouth and inhibit growth of harmful related Streptococcal bacteria, for example those causing sore throats (caused mainly by *S. pyogenes*). There is no teaching or suggestion in the specification that the *S. salivarius* will be useful against halitosis.

Applicants respectfully submit that one of skill in the art would not have expected that BLIS-producing *S. salivarius* would be useful in the treatment of halitosis because prior to the present invention it was unknown that BLIS-producing *S. salivarius* were active against bacteria other than closely related gram-positive bacteria. The enclosed §132 Declaration by inventor Dr. John Tagg (who is also the first named inventor on WO 01/27143) confirms that prior to the

present invention, it was unknown, and surprising, that *S. salivarius* could be used to treat halitosis. His expert view, as set forth in the Declaration, is that *S. salivarius* would only be active against closely related gram positive bacteria, for example *S. pyogenes* as cited in WO 01/27143. That is, it was very surprising to Dr. Tagg that BLIS-producing *S. salivarius* are active against unrelated bacteria including Eubacterium, Micromonas species, and anerobic gram-negative black-pigmented species. Organisms that are involved in halitosis occupy distinct niches in the oral cavity and are primarily producers of volatile sulphur compounds. Thus, Dr. Tagg did not expect that *S. salivarius* would be active against such organisms and able to treat halitosis caused by such organisms. See, Declaration at 8-14.

That is, nothing in WO 01/27143 teaches or suggests that BLIS-producing *S. salivarius* are active against Eubacterium, Micromonas species, and anerobic gram-negative black-pigmented species, and nothing in WO 01/27143 teaches or suggests that BLIS-producing *S. salivarius* can be used to treat halitosis. See, Declaration at 14-15.

The Office Action attempts to correct these deficiencies through the citations Huatan, Chikindas and Kross. Applicants respectfully submit that none of these references teach or suggest the pending claims, either alone or in any combination.

Turning first to Huatan, this reference relates to oral formulations with additives, specifically animal chews. Huatan uses such animal chews to deliver oral formulation.. The Office Action relies on Huatan as allegedly teaching “oral formulations which may comprises one or more medicaments including those for treating/preventing halitosis such as lantibiotics.” Office Action at 9. Specifically, the Office Action refers to Huatan at paragraphs 47 and 48.

In actuality, paragraph 48 of Huatan is a laundry list of possible medicaments as follows:

[0048] Examples of these medicaments may include anti-bacterial agents, wherein the agents (their analogues and salts) are derived from bis-guanidino antibacterials such as chlorhexidine, hexetidine, alexidine, etc.; myxovirescin; cetyl pyridinium chloride; minocycline, doxycycline, chlortetracycline and other tetracycline antibacterials; anionic antibacterials such as triclosan etc.; nisin and other lantibiotics; malabaricone C and other argingipain inhibitors; ofloxacin and other quinoline antibacterials; sulfaciazine; actinobolin; histatins, bactenecin and other peptide antibacterials.

(emphasis added).

Despite this passage in Huatan, there are no examples of any formulations with lantibiotics being produced, nor any evidence that such formulations were useful in controlling oral health, and more specifically treating halitosis. Lantibiotics are simply listed within a broad group of antibacterial agents. In contrast to the present invention, it is the lantibiotic *per se* that is contemplated for use in Huatan, not the administration of a bacteriocin producing *S. salivarius*, which will provide on-going release of the active form the bacterium into the oral cavity to treat halitosis. As stated in the background of the present specification at page 2, current methods of treating halitosis require complex physical, chemical or expensive regimes to be carried out with typically only a short term effect, as the malodour-causing oral bacteria recover to former levels after treatment has stopped. Applicants again direct the Examiner's attention to the accompanying Declaration, specifically paragraphs 16-19.

The present application seeks to treat halitosis by "the replacement of the disease-causing organisms, with a non-virulent commensal microorganism. To serve as an effector strain in replacement therapy, the microorganism must be able to compete successfully with the pathogenic microorganism either via competitive action (eg, for attachment sites), and/or antibiotic action, or inhibition via upper metabolism-associated by-products." See, specification at page 2, lines 9-13.

Huatan provides no teaching or suggestion of using bacteriocins producing organisms to achieve treatment of halitosis. It would not be apparent to a person skilled in the art following the teachings of Huatan that an *S. salivarius* BLIS-producing organism could be successfully introduced into the oral cavity to treat halitosis. Huatan therefore in no way compensates for the deficiency in WO 01/27143. The mere inclusion of lantibiotics in a laundry list is not sufficient to teach or suggest a bacteriocin producing *S. salivarius*. The selection of lantibiotics in the Office Action is mere cherry-picking, and is improper in the absence of some teaching directing the specific selection. As lantibiotics in general do not teach or suggest use of a bacteriocin producing *S. salivarius*, there is additionally no reason to combine Huatan with WO 01/27143.

The Office Action similarly alleges that Chikindas teaches "anti-microbial, anti-bad breath (halitosis) oral formulations which may comprise biomolecules such as bacteriocins as an active ingredient". Office Action at 9. Applicants disagree with this assertion.

Chikindas actually teaches formulations comprising histatins for the control of oral health conditions. As with Huatan, there is no teaching or suggestion of any compositions which

comprise the functional biomolecules, such as bacteriocins, antibodies, and enzymes, which are merely identified in the reference. As discussed in the accompanying Declaration at paragraph 22, the skilled artisan is only directed to use isolated active agents which operate by different mechanism of actions. It is not taught or suggested that bacteriocin is useful for treating halitosis. That is, there is nothing in Chikindas that would suggest the use of organisms in the oral cavity to produce bacteriocins, nor any mention of *S. salivarius* that could be effective against anaerobic halitosis causing organisms.

Turning now to Kross, the Office Action alleges that Kross “teaches treating an individual with halitosis/bad breath including the steps of scraping the tongue...followed by rinsing the mouth with an aqueous chlorine dioxide solution and/or with an acidic fruit juice.” Office Action at 9.

Applicants respectfully submit that Kross exemplifies the known art. This reference too fails to teach the key aspect of the Applicant's invention, namely the administration of *S. salivarius* bacteria which produce bacteriocins in the oral cavity and to treat halitosis. Chlorine dioxide treatment and pre-conditioning are a subsidiary aspect of the claims and are present only in dependent claims that all require the use of organisms in the oral cavity to produce bacteriocins.

As none of the cited references teach such a use of BLIS-producing *S. salivarius*, as is required by the pending claims, and as such a deficiency is not corrected by any combination of WO 01/27143, Huatan, Chikindas and Kross, the obviousness rejections cannot stand.

Thus, for all of these reasons, reconsideration and withdrawal of the rejections under 35 U.S.C. §§ 102 and 103 are respectfully requested.

IV. THE OBJECTION TO THE SPECIFICATION IS OVERCOME

The specification was objected to as failing to comply with the sequence requirements.

Applicants respectfully request acceptance of the enclosed paper copy and computer readable form of the Sequence Listing.

It is respectfully asserted that the sequence disclosure contained in the application now fully complies with the requirements set forth in 37 C.F.R. § 1.821 to § 1.825. The Statements required by 37 C.F.R. §1.821(f) and (g) are set forth below.

Pursuant to 37 C.F.R. §1.821 (g), the undersigned hereby states that this submission, filed in accordance with 37 C.F.R. §1.821 (g), does not contain new matter.

Pursuant to 37 C.F.R. §1.821 (f), the undersigned hereby states that the content of the paper and computer readable copies of the Sequence Listing submitted in accordance with 37 C.F.R. §1.821 (c) and (e), respectively, are the same. No new matter is added.

Applicants respectfully submit that the requirements of the Notice are now met. Accordingly, reconsideration and withdrawal of the Notice to Comply is respectfully requested.

REQUEST FOR INTERVIEW

If any issue remains as an impediment to allowance, an interview with the Examiner is respectfully requested, prior to issuance of any paper other than a Notice of Allowance; and, the Examiner is respectfully requested to contact the undersigned to arrange a mutually convenient time and manner for such an interview.

CONCLUSION

In view of the remarks and amendments herewith and those of record, the application is in condition for allowance. Favorable reconsideration of the application and prompt issuance of a Notice of Allowance, or an interview at a very early date with a view to placing the application in condition for allowance, are earnestly solicited. The undersigned looks forward to hearing favorably from the Examiner at an early date.

Respectfully submitted,

FROMMER LAWRENCE & HAUG LLP
Attorneys for Applicants

By: /Angela M. Collison/
Marilyn Matthes Brogan
Reg. No. 31,223
Angela M. Collison
Reg. No. 51,107
Tel. (212) 588-0800